13 Mannose binding lectin gene as a modifier of cystic fibrosis phenotype in Argentinian pediatric patients

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Introduction: Mannose binding lectin (MBL) is an innate immune protein. It has been proposed as a modulator of severity in cystic fibrosis (CF), since lung infections are the main cause of morbility and mortality in this disease.
Objectives: To investigate the influence of MBL2 structural and promoter variants on disease severity in CF patients.
Patients and Methods: One hundred and six CF patients carrying two severe mutations in the CFTR gene were retrospectively evaluated. MBL2 structural and promoter variants were studied by PCR-RFLP. YA/YA, YA/XA genotypes were considered as MBL sufficient (MBL-S) and XA/XA, YA/0, XA/0, 0/0, MBL insufficient (MBL-I). Clinical phenotype of patients between 5–9 years old (n = 66) was defined as severe, moderate and mild according to Schawman score. Pulmonary function tests (FEV_1) were performed in children over 6 years old and age of first positive culture of *Pseudomonas aeruginosa* (*P.a.*) was registered.
Results: Based on genotype, patients were stratified into two groups: MBL-S (n = 57) and MBL-I (n = 49). MBL insufficiency was associated with a 3.5-fold risk of having a severe phenotype (95% CI 1.2–10.3). It was also associated with an earlier onset of infection with *P.a.* ($p = 0.03$). No difference was found in FEV_1 at age of 7. In the follow up, FEV1 of MBL-I patients was below the MBL-S group. Global survival was reduced in the MBL-I group, even though this difference was not significant.
Conclusions: In this study population, MBL insufficiency was associated with a poor prognosis in children with CF. These findings suggest MBL as a modulating factor in this genetic disease.

14 Polymorphisms c.1408A>G (Met470Val), c.2562T>G and c.4389G>A and their haplotypes and clinical features of CF

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Aim of the study: In presented study the frequencies of *CFTR* mutation and three SNP are studied: c.1408A>G in exon 10 (Met470Val, rs213950), c.2562T>G in exon 14b (rs1042077) and c.4389G>A in exon 24 (rs1800136).
Materials and Methods: The haplotypes of those three SNP are also studied along with clinical symptoms and microbiological data of 145 CF patients and 141 healthy subjects. The genotyping was performed using Real Time-PCR on AB 7900HT apparatus and confirmed by direct sequencing.
Results: The results of the conducted studies indicate that genotypes of GG of c.1408A>G, TT of c.2562T>G and GG of c.4389G>A are statistically more frequent in CF patients. Moreover the most frequent haplotype formed by these SNPs is GTG observed in 48.7% of patients. GG genotype of c.1408A>G SNP is correlated with pancreatic insufficiency, lower concentration of fecal elastase-1 and earlier *S. aureus* colonization (of 1.5 year), c.2562T>G SNP genotyping alone has no clinical relevance, GG genotype of c.4389G>A SNP is correlated with digital clubbing, pancreatic insufficiency, lower concentration of fecal elastase-1 and earlier *S. aureus* colonization (of 1 year). Finally, GTG haplotype formed by three studied SNPs is correlated with higher chloride concentration in Wescor sweat test, pancreatic insufficiency, higher cholecalcipherol concentration is plasma with earlier colonization caused by *S. aureus* (of 1 year).
Conclusion: Our observations suggest that selected SNPs and their haplotypes may determine some of the clinical features of cystic fibrosis, and what is most important they influence on the age of acquiring of chronic *S. aureus* colonization.